

We Claim:

1. A composition of compounds effective for treating a pathology, said composition comprising at least two compounds that modulate the activity of one or more target molecules associated with one or more Single Nucleotide Polymorphisms (SNPs), wherein each compound modulates the activity of at least one target molecule associated with one or more SNPs, and wherein said combination is effective for at least one patient having said pathology.

2. The composition of claim 1 wherein said combination is effective for at least 1% of patients having said pathology.

3. The composition of claim 1 wherein said combination is effective for at least 25% of patients having said pathology.

4. The composition of claim 1 wherein said combination is effective for at least 50% of patients having said pathology.

5. The composition of claim 1 wherein said combination is effective for at least 75% of patients having said pathology.

6. The composition of claim 1 wherein said combination is effective for at least 90% of patients having said pathology.

7. The composition of claim 1 wherein said compound interacts with said target molecule at a position corresponding to said SNP or at a position corresponding to a residue encoded by a codon comprising said SNP.

8. The composition of claim 1 wherein said composition comprises at least three compounds.

9. The composition of claim 1 wherein said composition comprises at least four compounds.

5 10. The composition of claim 1 wherein said composition comprises at least five compounds.

11. The composition of claim 1 wherein said composition comprises at least six compounds.

10 12. A composition of compounds effective for treating a pathology, said composition comprising at least two compounds that modulate the activity of at least one target molecule associated with at least one SNP, wherein said combination is effective for at least one patient having said pathology.

15 13. The composition of claim 12 wherein the modulation effect of each compound is correlated with the presence of the same SNP associated with the same target molecule.

14. The composition of claim 12 wherein the modulation effect of each compound is correlated with the presence of a mutually exclusive SNP associated with the same target molecule.

20 15. The composition of claim 14 wherein said mutually exclusive SNPs occur in a single patient.

16. The composition of claim 14 wherein said mutually exclusive SNPs occur in a plurality of patients.

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17. The composition of claim 12 wherein the modulation effects of said compounds are correlated with the presence of a SNP on at least two target molecules.

18. The composition of claim 17 wherein at least one
5 target molecule is associated with at least two SNPs.

19. The composition of claim 18 wherein at least two target molecules are associated with at least two SNPs.

20. A composition of compounds effective for treating a pathology, said composition comprising at least two compounds that modulate the activity of a single target protein associated with one or more SNPs, wherein said combination is stably effective for at least one patient having said pathology.

21. The composition of claim 20 wherein the modulation effect of each compound is correlated with the presence of the same SNP associated with said target protein.

22. The composition of claim 20 wherein the modulation effect of each compound is correlated with the presence of a mutually exclusive SNP associated with said target protein.

23. The composition of claim 20 wherein said
20 composition comprises at least three compounds.

24. The composition of claim 20 wherein said composition comprises at least four compounds.

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25. The composition of claim 20 wherein said combination is stably effective for at least 50% of patients having said pathology.

5 26. The composition of claim 20 wherein said combination is stably effective for at least 75% of patients having said pathology.

27. The composition of claim 20 wherein said combination is stably effective for at least 90% of patients having said pathology.

10 28. A method of increasing overall treatment efficacy for a given population of patients having a pathology, comprising:

(a) analyzing compounds known or suspected of modulating the activity of at least one target molecule corresponding to said pathology for efficacy correlated with the presence of a SNP associated with said target molecule(s); and

15 20 (b) selecting, for treatment of said patients, a combination of at least two of said compounds that exhibit the highest overall mean response of all dosing options in said population of patients.

29. The method of claim 28 wherein said combination is effective for at least 25% of said patients.

25 30. The method of claim 28 wherein said combination is effective for at least 50% of said patients.

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31. The method of claim 28 wherein said combination is effective for at least 75% of said patients.

32. The method of claim 28 wherein said combination is effective for at least 90% of said patients.

5 33. A method of maximizing overall population efficacy of treatment for a particular pathology, comprising:

(a) determining the efficacies of a plurality of compounds known or suspected of treating said pathology;

(b) determining the toxicity of said plurality of compounds; and

(c) selecting from said plurality of compounds a combination of compounds that is minimally toxic and is effective for at least 1% of the total patient population having said pathology.

34. A method of formulating a pharmaceutical composition for treating a particular pathology in a population of patients having said pathology, comprising:

(a) measuring a correlation of genetic variation of a target molecule in said population with patient response to at least one compound known or suspected to treat said pathology; and

(b) selecting at least two compounds that provide the greatest percentage of efficacy in said patient

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population, wherein said percentage is at least 1% of the total patient population having said pathology.

35. The method of claim 34 wherein said composition comprises at least three compounds.

5 36. The method of claim 34 wherein said composition exhibits minimal toxicity.

37. The method of claim 34 wherein said composition exhibits no toxicity.

38. A genotypically-facilitated method of treating one or more patients having a pathology, comprising:

(a) analyzing a therapeutic target molecule in a population of patients having said pathology to detect SNPs associated therewith;

(b) selecting a plurality of compounds having therapeutic efficacies correlated with the presence of at least one SNP associated with said target molecule; and

(c) administering said plurality of compounds to a patient in said population;

20 wherein said combination is effective for at least 1% of the total patient population having said pathology.

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39. The method of claim 38 wherein said plurality of compounds is administered to said patient simultaneously or proximately to one another.

40. A method of formulating a therapeutic composition to treat a pathology, comprising:

(a) analyzing a target molecule in a patient population to detect SNPs associated therewith; and

(b) selecting a plurality of compounds having therapeutic efficacies correlated with the presence of at least one SNP associated with the target molecule, wherein said plurality is effective for at least 1% of the total patient population having said pathology.

41. A method of selecting an optimized therapeutic composition to treat a pathology, comprising selecting a combination of at least two compounds that exhibits the highest overall mean response of all dosing options and exhibits the lowest variation in response across different population groups, wherein said combination is effective for at least 1% of the total patient population having said pathology.

42. The method of claim 41 wherein a total dosage of said composition does not exceed a threshold for toxicity.

43. A method of preparing an optimized pharmaceutical composition, comprising identifying a combination of at least two compounds that exhibit maximal population efficacy across all known SNPs associated with a particular target molecule

correlated with a pathology, wherein said combination exhibits minimal toxicity.

44. The method of claim 43 wherein said combination is effective for at least 25% of patients having said pathology.

5 45. The method of claim 43 wherein said combination is effective for at least 50% of patients having said pathology.

46. The method of claim 43 wherein said combination is effective for at least 75% of patients having said pathology.

47. The method of claim 43 wherein said combination is effective for at least 90% of patients having said pathology.

48. A method of optimizing therapeutic treatment of a pathology, comprising selecting a combination of compounds that minimize overlap of drug efficacy in patients having said pathology, wherein said combination of compounds exhibits minimal toxicity.

49. The method of claim 48 wherein said combination is effective for at least 25% of patients having said pathology.

50. The method of claim 48 wherein said combination is effective for at least 50% of patients having said pathology.

20 51. The method of claim 48 wherein said combination is effective for at least 75% of patients having said pathology.

52. The method of claim 48 wherein said combination is effective for at least 90% of patients having said pathology.

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53. A method of treating a sub-population of patients having a particular pathology, comprising:

5 (a) identifying a sub-population of patients having at least one known SNP from all patients exhibiting said pathology; and

(b) administering to said sub-population a composition comprising at least one therapeutic compound having an efficacy correlated with the presence of said SNP.

54. A method of treating a sub-population of patients having a particular pathology, comprising:

(a) identifying a sub-population of patients having a known SNP profile from all patients exhibiting said pathology; and

(b) administering to said sub-population a composition comprising at least one therapeutic compound having an efficacy correlated with said SNP profile.

55. A method of preparing a combination of compounds for treating one or more patients having a pathology, wherein said combination of compounds has increased efficacy and/or reduced toxicity, relative to any individual compound, in a greater portion of a population of patients having said pathology, comprising:

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(a) correlating the efficacy and/or toxicity of a first compound with the presence of one or more SNPs;

(b) correlating the efficacy and/or toxicity of a second compound with the presence of one or more SNPs; and

(c) calculating the efficacy and/or toxicity of a combination of said first compound and said second compound on said population of patients;

wherein said combination is effective for at least 1% of the total patient population having said pathology.

56. The method of claim 55, further comprising the steps of:

(d) correlating the efficacy and/or toxicity of a third compound with the presence of one or more SNPs; and

(e) calculating the efficacy and/or toxicity of a combination of said first compound, said second compound and said third compound on said population of patients.

57. An algorithm for determining the efficacy and/or toxicity of a combination of two or more compounds for a population of patients having a pathology, comprising the steps of:

(a) correlating the efficacy and/or toxicity of each of said two or more compounds with the presence of one or more SNPs; and

(b) combining the correlations of the efficacy and/or toxicity of each of said two or more compounds with the presence of one or more SNPs;

whereby the efficacy and/or toxicity of said combination of compounds for said population of patients is calculated.

58. A method of treating a patient having a pathology with a combination of therapeutic compounds having increased efficacy and/or reduced toxicity, relative to any individual compound, in a greater portion of a population of patients having said pathology, comprising the steps of:

(a) correlating the efficacy and/or toxicity for each of two or more compounds with one or more SNPs;

(b) calculating the efficacy and/or toxicity of administering said two or more compounds on said population of patients; and

(c) administering said two or more compounds to said patients;

wherein said two or more compounds are effective for at least 1% of the total patient population having said pathology.

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59. The method of claim 57 wherein each of said two or more compounds is administered to said patient simultaneously or proximately to one another.

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